REMARKS

Claims 17, 18, 33-36, and 49 have been amended to improve antecedent basis and to improve the clarity of the claims. Claim 23 has been amended to correct the dependency of the claim.

The Office Action mailed July 1, 2005, has been received and reviewed. Claims 17-21, 23-27, 29-31, 33-41, and 49-53 are currently pending in the application. Claims 17-21, 23-27, 29-31, 33-41, and 49-53 stand rejected. Applicants have amended claims 17, 18, 23, 33-36, and 49 and respectfully request reconsideration of the application as amended herein.

35 U.S.C. § 103(a) Obviousness Rejections

Obviousness Rejection Based on U.S. Patent No. 4,376,118 to Daher *et al.* in view of U.S. Patent No. 5,284,655 to Bogdansky *et al.*

Claims 17-21, 23-27, 29-31, 33-41, and 49-53 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 4,376,118 to Daher *et al.* ("Daher") in view of U.S. Patent No. 5,284,655 to Bogdansky *et al.* ("Bogdansky"). Applicants respectfully traverse this rejection, as hereinafter set forth.

M.P.E.P. 706.02(j) sets forth the standard for an obviousness rejection:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

The obviousness rejection of claims 17-21, 23-27, 29-31, 33-41, and 49-53 is improper because the cited references do not provide a motivation to combine to produce the claimed invention.

Daher teaches a nonaqueous solution of a tetracycline antibiotic salt. Daher at column 1,

lines 35-39. The solution includes a tetracycline salt, a nonaqueous diluent, a nonaqueous solvent, a nonaqueous nonionic solubilizer, an antioxidant, and a nonaqueous anionic solubilizer. *Id.* at column 1, lines 35-41. The nonaqueous solution includes lauryl lactate as the nonaqueous diluent, ethylene oxide propylene oxide block copolymers and polysorbate as the nonaqueous nonionic solubilizer, and ethanol, methanol, or N-methyl-2-pyrrolidone as the solvent. *Id.* at column 1, lines 51-64 and column 2, lines 3-10. The nonaqueous solution is prepared by mixing the nonaqueous nonionic solubilizer and the nonaqueous anionic solubilizer with the nonaqueous solvent at ambient room temperature. *Id.* at column 2, lines 48-53. These ingredients are mixed until they are dissolved. *Id.* The tetracycline antibiotic salt and the antioxidant are then added with mixing, followed by addition of the nonaqueous diluent. *Id.* at column 2, lines 53-56. The nonaqueous solution is applied topically to provide therapeutic activity as an antibiotic. *Id.* at column 7, lines 45-63.

Bogdansky teaches an osteogenic composition that includes swollen demineralized bone particles and a biocompatible fluid carrier. Bogdansky at column 1, lines 18-23. The osteogenic composition includes autogenous, allogenic, or xenogenic bone tissue and a polyhydroxy compound, such as glycerol monolaurate, as the biocompatible fluid carrier. *Id.* at column 1, lines 42-45 and column 3, line 61 through column 4, line 52. The osteogenic composition also includes polyvinylpyrrolidone, proteins, or antibiotics, such as tetracycline, to modify the characteristics of the osteogenic composition. *Id.* at column 5, line 26 through column 6, line 11. The swollen demineralized bone particles are prepared by exposing demineralized bone particles to a liquid swelling agent, which is subsequently removed before suspending the swollen demineralized bone particles in the biocompatible fluid carrier. *Id.* at column 3, lines 45-59 and column 5, lines 1-7. The osteogenic composition is applied to an osseous defect by packing to cause new bone ingrowth. *Id.* at column 1, line 67 through column 2, line 4. The osteogenic composition has a paste- or putty-like consistency or a liquid consistency. *Id.* at column 2, lines 19-26.

Independent claim 17 recites a formulation that comprises at least one beneficial agent and a non-aqueous, single-phase biocompatible vehicle. The beneficial agent is selected from the group consisting of a peptide, a protein, a nucleotide, a hormone, a virus, an antibody, and

analogs, derivatives, or pharmaceutically acceptable salts thereof. The non-aqueous, single-phase biocompatible vehicle comprises a solvent, a surfactant, and a polymer, wherein the solvent is lauryl lactate. The solvent, the surfactant, and the polymer are selected and formulated such that the non-aqueous, single-phase biocompatible vehicle exhibits a viscosity capable of suspending the at least one beneficial agent.

The cited references do not provide a motivation to combine to produce the invention of independent claim 17. To provide a motivation or suggestion to combine, the prior art or the knowledge of a person of ordinary skill in the art must "suggest the desirability of the combination" or provide "an objective reason to combine the teachings of the references." M.P.E.P. § 2143.01. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *Id.* (emphasis in original). "[I]t is fundamental that rejections under 35 U.S.C. § 103 must be based on evidence" and that the evidence "must be based on objective evidence of record." *In re Lee*, 61 U.S.P.Q.2d 1430, 277 F.3d 1338, 1342-1343 (Fed.Cir. 2002). In other words, the motivation to combine can not "be resolved on subjective belief and unknown authority." *Id.* at 1344. In addition, the Examiner "cannot rely on conclusory statements when dealing with particular combinations of prior art and specific claims, but must set forth the rationale on which it relies." *Id.* at 1345.

As acknowledged by the Examiner, Daher does not teach or suggest a beneficial agent as recited in claim 17. Office Action of July 1, 2005, p. 3. Therefore, the Examiner relies on Bogdansky as teaching this limitation and states that "[p]rotein and tetracycline are equivalent as active agents in Bogdansky." *Id.* However, this statement by the Examiner is conclusory and is not based on objective evidence of record. The Examiner appears to equate the equivalence of proteins and tetracycline merely on the fact that both substances are taught as being medically or surgically useful substances in the osteogenic composition of Bogdansky. However, the mere fact that these two substances are medically or surgically useful in a composition that causes bone growth would not suggest to one of ordinary skill in the art the desirability of combining Daher and Bogdansky to produce the claimed invention, or provide an objective reason for doing so. As previously discussed, Daher is limited to teaching a nonaqueous, antibiotic solution that

includes a tetracycline salt. Nothing in Daher suggests the desirability of, or provides an objective reason for, using other beneficial agents in its nonaqueous solution, such as one of the beneficial agents recited in claim 17. Since the teachings of Daher are limited to a nonaqueous solution of a tetracycline salt, Daher is completely silent regarding additional active agents or compounds. Bogdansky also does not suggest the desirability of, or provide an objective reason for, using proteins in other compositions, such as in the nonaqueous, antibiotic solution of Daher. Rather, Bogdansky only teaches that proteins are useful in its osteogenic composition.

Since the cited references do not provide a motivation to combine to produce the claimed invention, the obviousness rejection of claim 17 is improper and should be withdrawn.

Claims 19-21, 23-27, 29-31, and 49-53 are allowable, *inter alia*, as depending from an allowable base claim, namely claim 17.

Claim 27 is further allowable because the cited references, when combined, do not provide any motivation to produce a formulation for use in an implantable drug delivery device, as discussed below in regard to claim 33.

Independent claim 18 is directed to a non-aqueous formulation and recites substantially the same limitations as claim 17. Therefore, claim 18 is allowable for substantially the same reasons as discussed above for claim 17.

Independent claim 33 is directed to a method of preparing a formulation and recites, *inter alia*, limitations that are substantially similar to those recited in claim 17. Therefore, claim 33 is allowable for substantially the same reasons as discussed above for claim 17.

The Examiner also states that "it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the tetracycline formulation of Daher. One having ordinary skill in the art would have been motivated to substitute protein for tetracycline with the expectation that the protein containing formulation would be flowable and suitable for implantation or injection." Office Action of July 1, 2005, p. 4. However, this reasoning by the Examiner is conclusory and is not based on objective evidence of record. Contrary to the Examiner's assertion, one of ordinary skill in the art would not have expected a protein-containing formulation produced by the combination of Daher and Bogdansky to be suitable for implantation or injection because the osteogenic composition of Bogdansky is applied directly to

the osseous defect and the tetracycline composition of Daher is applied topically. Therefore, nothing in Daher and Bogdansky, when combined, provides any motivation to produce a formulation suitable for implantation or injection.

In addition, Applicants respectfully submit that the Examiner has mischaracterized the teachings of Bogdansky by stating that the osteogenic composition of Bogdansky "can be administered by injection, a parenteral administration." *Id.* The section of Bogdansky relied upon by the Examiner in support of this statement actually teaches that bone particles are demineralized by various steps, such as treating the bone particles with acid and water. The water used as one of the ingredients in these treatments is referred to as "water for injection." See Bogdansky at column 2, line 67 through column 3, line 4. However, nothing in Bogdansky teaches that the osteogenic composition is administered by injection. Rather, Bogdansky clearly discloses that its osteogenic composition is applied to the osseous defect by packing the osseous defect with the osteogenic composition.

Claims 34 and 35 are allowable, *inter alia*, as depending from an allowable base claim, namely claim 33.

Independent claim 36 is directed to a method of treating a subject and recites, *inter alia*, limitations that are substantially similar to those recited in claim 17. Therefore, claim 36 is allowable for substantially the same reasons as discussed above for claim 17.

Claims 37-41 are allowable, *inter alia*, as depending from an allowable base claim, namely claim 36.

Claims 37 and 39 are further allowable because, as discussed above, the cited references do not provide any motivation for parenteral administration or using an implantable drug delivery system because the tetracycline composition of Daher is applied topically and the osteogenic composition of Bogdansky is directly packed against the osseous defect.

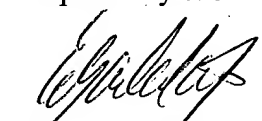
ENTRY OF AMENDMENTS

The amendments to claims 17, 18, 23, 33-36, and 49 above should be entered by the Examiner because the amendments are supported by the as-filed specification and drawings and do not add new matter to the application.

CONCLUSION

Claims 17-21, 23-27, 29-31, 33-41, and 49-53 are believed to be in condition for allowance, and an early notice thereof is respectfully solicited. Should the Examiner determine that additional issues remain that might be resolved by a telephone conference, the Examiner is respectfully invited to contact Applicants' undersigned attorney.

Respectfully submitted,



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Date: October 3, 2005
ERC/KAH/dlm:es

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